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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/991,628	11/05/97	STOMINGER J	HAR-001DV

EXAMINER	
DIBRINO, M	
ART UNIT	**PAPER NUMBER**
1644	20

DATE MAILED: 07/03/00

HM22/0703

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.	Applicant(s)
09/991,628	Strominger et al.
Examiner	**Group Art Unit**
Marianne DiBrino	1644

☒ Responsive to communication(s) filed on *Apr 13, 2000*

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *3-6, 11, and 13-16* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *3-6, 11, and 13-16* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *13*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. The Art Unit location and the examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1644.

2. Applicant's amendment, filed 4/13/00 (Paper No. 18), is acknowledged and has been entered.

Claims 3-6, 11 and 13-16 are pending and are presently being acted upon.

The following are new grounds of rejection necessitated by the amendment filed 4/13/00.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 3-6, 11 and 13-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 3-6, 11 and 13-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical preparation comprising a human polypeptide consisting of one of SEQ ID NOS: 1-7, does not reasonably provide enablement for the claimed pharmaceutical preparation comprising a human polypeptide *consisting essentially of* an amino acid sequence corresponding to the core MHC binding residues of a sequence motif for an HLA-DR protein, nor consisting essentially of one of SEQ ID NOS: 1-7, nor a polypeptide *having* an amino acid sequence *corresponding* to the core MHC binding residues of a sequence motif for an HLA-DR protein. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification does not disclose how to make/and or use a pharmaceutical preparation comprising a human polypeptide *consisting essentially of* an amino acid sequence corresponding to the core MHC binding residues of a sequence motif for an HLA-DR protein, nor *consisting essentially of* one of SEQ ID NOS: 1-7, nor a polypeptide *having* an amino acid sequence *corresponding* to the core MHC binding

residues of a sequence motif for an HLA-DR protein. The specification has not enabled the breadth of the claimed invention in view of the teachings of the specification because the claims encompass amino acid residues in the P1-P9 "core" that are non-HLA-DR binding amino acid residues at HLA-DR motif binding positions and additionally encompass proteinaceous material which contains sequences outside of the "core" MHC binding residues of a sequence motif for an HLA-DR protein.

The specification does not define the term "human polypeptide *consisting essentially of* an amino acid sequence corresponding to the core MHC binding residues of a sequence motif for an HLA-DR protein." The specification on page 52 at lines 25-27 discloses that the term "core MHC binding residues" means the residues of an epitope corresponding to the P-1 to P-9 positions of a peptide bound to an HLA-DR molecule. The specification further discloses that there are 5 binding pockets in MHC (class II, DR), P1, P4, P6, P7 and P9 (page 19 at lines 17-25), at least two of which (page 19 at lines 29-31, page 20, lines 5-6) are used via consideration of the chemical nature and size of said binding pockets (page 20 at lines 9-23) for determination of the sequence motif of the corresponding peptide that binds to the MHC molecule (page 19 at lines 29-31).

Accordingly, the amino acids at a maximum of three of the motif positions may not be motif amino acids and may actually be deleterious to binding. The PV motif #1 of instant claim 5 has only three defined positions, P1, P4 and P6. O'Sullivan (1991) was relied upon in a previous office action mailed 6/16/99 for the teaching that the presence of putative binding motif residues does not necessarily correlate with actual binding to an MHC molecule because both binders and nonbinders may have the putative motif (last sentence in Abstract). In addition, the amino acid residues outside the "core" may also be deleterious to binding.

There is no guidance in the specification as to what alterations result in a functional polypeptide, i.e., one that binds to HLA-DR. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain functional activity, and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e., its activity) are not well understood and are therefore not predictable (Ngo et al. The Protein Folding Problem and Tertiary Structure Prediction, Merz & LeGrand, Birkhauser Boston, pages 491-495, 1994, entire article, especially Section 6, paragraph 1), it would require undue experimentation for one of skill in the art to arrive at other amino acid sequences that would have functional activity. In other words, since it would require undue experimentation to identify amino acid sequences that have functional

activity, it would require undue experimentation to make the corresponding sequences. The enablement provided by the specification is not commensurate with the scope of the claims.

With regard to Applicant's comments on O'Sullivan in the amendment filed 4/13/00, Applicant's assert that the binding motif of the present invention characterizes five MHC contact residues and six T cell receptor contact residues (page 7, 2nd paragraph, lines 6-8) and that Sullivan relied upon a three-residue binding motif. As discussed supra, Applicants claims encompass a two- residue binding motif.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 13-16 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 13 is indefinite in the recitation of "wherein said preparation is *free* of a polypeptide corresponding to said sequence" because it is not clear what is meant. The instant claim 13 recites a pharmaceutical preparation comprising an amount of an immunogenic preparation effective to immunize against a human pathogen that in its native form *includes* a polypeptide that has a sequence that binds to an HLA-DR protein.

b. Claim 13 is indefinite in the recitation of "includes a polypeptide" because it is not clear whether said polypeptide is a portion of a protein from a pathogenic organism.

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 3-6 and 13-16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 3 of U.S. Patent No. 5,874,531. Although the conflicting claims are not identical, they are not patentably distinct from each other because the composition comprising the peptides of claim 3 of the '531 patent are encompassed by the instant claims.

In view of the amendment filed 4/13/00 only the following rejection remains.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 3-5 and 13-15 stand rejected under 35 U.S.C. 102(b) as being anticipated by Amagai et al (Cell, Vol. 67, pages 869-877, 1991) for the reasons of record in Paper No. 12 mailed 6/16/99.

Applicant's arguments filed 4/13/00 have been fully considered but they are not persuasive.

With regard to Applicant's comments on pages 8 and 9 of said amendment, it is Applicant's position that the term "consisting essentially of" limits the scope of the claims. However, in the absence in the specification of a definition of "human polypeptide consisting essentially of...", the claim language is open, and inclusive of the full-length autoantigen.

With regard to Applicant's comments about instant claims 13-16, on page 9 of said amendment at the last paragraph, Applicant's comments do not make sense because Applicant asserts that "Independent claim 13 recites, in part, a vaccination preparation that in its native preparation includes a polypeptide having an amino acid sequence corresponding to a sequence motif for an HLA-DR protein...wherein said preparation is free amino acid sequence corresponding to a sequence motif for an HLA-DR protein." With regard to Applicant's comments in the last 4 lines of said paragraph, the instant claim 13-16 do not recite a vaccination preparation which includes antigenic polypeptides of a pathogen and excludes polypeptides that activated autoreactive T cells from a subject having an autoimmune disease.

11. No claim is allowed.

2. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marianne DiBrino whose telephone number is (703) 308-0061. The examiner can normally be reached Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

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